COMMENTARY

Environmental Estrogens: Health Implications for Humans and Wildlife

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Recent efforts to increase communication among specialists from a wide range of disciplines has led to a better understanding of the scope and magnitude of the geographic distribution and effects of synthetic chemicals. Cross-discipline research has improved detection of widely dispersed chemicals that are capable of disrupting the endocrine system and/or interfering with reproduction. Reviewing what is known about the effects of xenobiotics from the molecular, cellular, tissue, and organismal levels in relation to effects reported at the population level provides insight about functional changes that are often not visible and are difficult to determine. By adding a wildlife component to these analyses, a clearer picture of the nature of endocrine disruption has been demonstrated. Parallels among laboratory, human, and wildlife studies provide guidance for further multidisciplinary and interagency research. Movement toward forensic research among federal agencies responsible for human and environmental health will lead to increased knowledge about the role of endocrine disruptors in the environment.

The following statements were published in the peer-reviewed literature in 1981 by John McLachlan, Retha Newbold, Ken Korach, Jim Lamb, and Yoshihide Suzuki (*1*). The same words apply today to the third conference on "Estrogens in the Environment."

> In recent years there has been a growing concern about the exposure of pregnant women to drugs or chemicals and the subsequent effects on their offspring...[F]unctional abnormalities of the immune system, neurological defects, or appearance of tumors that are noticed in adult life may be linked to exposure to toxic agents in the prenatal period...For example, the development of the genital tract and subsequent attainment of fertility is a process susceptible to disruption by environmental agents.

The prescience of these words has been confirmed repeatedly over the past decade. For example, 11 years after the McLachlan et al. paper (*1*) was published, a team of reproductive specialists in Denmark startled the world with the announcement in the *British Medical Journal* that sperm counts had dropped approximately 50% since 1938 in the industrialized world (*2*). In response to the paper, scientists in this country and Europe have stated that the cause of this threat to male fertility may be due in part to exposure to elevated concentrations of estrogens or estrogenlike substances during embryonic, fetal, and early postnatal development. Since the mid-1940s, human exposure to xenobiotics during these critical periods of development has become widespread, reaching to all geographic regions. Endocrine-disrupting chemicals have been reported in semen, the ovarian follicle, the womb environment, and in breast milk at especially elevated concentrations, each chemical with its own mix of mechanisms of actions and unique target sites (*3*).

Significant advances in understanding the mechanisms of action of environmental estrogens emerged from two earlier conferences sponsored by McLachlan and his team: "Estrogens in the Environment I" in 1979, and "Estrogens in the Environment II" in 1983. Within the past decade, however, knowledge about "environmental hormones" has evolved more rapidly because of research that bridged disciplines and brought unique groups of individuals together. As this cross-discipline research progressed, its heuristic nature led to investigations that are more in the realm of scientific detective work, sometimes called forensic science. The papers that follow this commentary are examples of this kind of science. They serve as models and guideposts for moving forward with efforts to learn more about the role of synthetic chemicals in the environment.

Perhaps, the most distinguishing aspect of this conference in a historical context is the acceptance that evidence of damage in wildlife is relevant to human health. Most important are the parallels reported across vertebrate species of the effects of endocrine disruptors at each level of biological organization—from the molecule, to the cell, to tissues, organs, organisms, and populations.

Because the damage from exposure to endocrine disruptors is most often not visible, it can be missed until it has affected a large number of individuals, e.g., the worldwide reduction in human sperm quality and quantity. Here again, wildlife can increase our insight about the role of environmental contaminants during development. With shorter generation times than humans, wildlife could provide clues concerning the invisible, long-term effects of transgenerational exposure to endocrine disruptors before the effects become pervasive and are manifested in human populations. The real test now is whether those charged with protecting human and wildlife health understood the messages from this conference and have the courage and resources to make necessary changes. It is imperative that the institutions charged with protecting human and ecosystem

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health realign their research agendas to deal with chemicals that have slipped through the safety net of modern toxicology. To do this, the focus of future research agendas must broaden and move beyond acute toxicity and the cancer risk paradigm and incorporate the forensic approach. For the sake of future generations of humans and wildlife, gene expression and differentiation explored through multiagency and multidisciplinary research must be accommodated by the federal agencies responsible for human and ecological health.

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